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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,092	05/25/2006	Steven F. Dowdy	1034123-000199	9450

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EXAMINER	
DESAI, ANAND U	
ART UNIT	**PAPER NUMBER**
1656	

NOTIFICATION DATE	DELIVERY MODE
09/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/561,092	DOWDY ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29 and 31-36* is/are pending in the application.

4a) Of the above claim(s) *5,7-10 and 20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,11-19 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20070611*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on June 11, 2007. Claim 30 has been cancelled. New claim 36 has been added. Claims 5, 7-10, 20-29 have been withdrawn previously. Claims 1-4, 6, 11-19, 31-36 are currently pending and are under examination.

Maintenance of Rejections

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4, 6, 11-19, 32, and 33 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was explained in the office action mailed March 7, 2007.

Response to Remarks

4. Applicants' state the claims refer to "protein transduction moiety" to identify a class of agents capable of traversing the cell membrane. This genus is well recognized in the art and includes a number of existing and easily identified species. Thus, Applicants' disclosure reasonably conveys a genus of PTDs known or identifiable in the art. Applicants' cite Falkner v. Inglis to state the neither examples or DNA sequence are required to provide an adequate written

description to support a claim for proxvirus, as articles contemporaneous with the filing date showed relevant genes and nucleotide sequences to demonstrate knowledge to those skilled in the art. Applicants submit the term protein transduction domain and PTD are known in the art to refer to a class of polypeptides and that such polypeptides are known based upon contemporaneous articles. Applicants' state the one of skill in the art can identify new and newly developed protein transduction domains using methods and techniques known to those of skill in the art citing Table 1 at page 22-24. Applicants' state the disclosure provides species of protein transduction domains and functional fragments thereof citing paragraphs [0041] and [0062]. Applicants' state that a large number of heterologous polypeptides have been demonstrated as being capable of conjugation/linking to a protein transduction moiety citing Table 1 at pages 22-24. Applicants' state the claims refer to "fusogenic protein" to identify a class of proteins that facilitates the destabilization of a cell membrane or the membrane of a cell organelle. Applicants' state they provide a number of fusogenic polypeptides that can be used in the methods and compositions of the invention. Applicants' state the hemagglutinin influenza is a polypeptide. Applicants' cite various viral glycoproteins, such as the transmembrane glycoproteins of the Marburg virus, the Ebola virus, the rabies virus, and vesicular stomatitis virus. Applicants' state the genus of fusogenic moieties is well recognized in the art and includes a number of existing and easily identified species. Applicants submit that the term fusogenic polypeptide is known in the art to refer to a class of polypeptides and that such polypeptides are known based upon contemporaneous article. Applicants' cite Bullok et al. and Trehin et al. to demonstrate translocation across cell membranes. Applicants' state the reliance

upon Violini et al. and Falnes et al. for the teaching that the invention was not in Applicants' position at the time of filing is in error.

Applicant's arguments filed June 11, 2007 have been fully considered but they are not persuasive. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of genus of fusion polypeptides beyond those disclosed in the examples in the specification.

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Falnes et al. does not detect translocation in the cytosol state for a TAT-dtA fusion protein (see page 4351, col. 2, Results section, 2nd indented paragraph, 2nd to last sentence, and Figure 2, lack of toxicity with TAT-dtA construct).

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the

specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

5. Claims 1-4, 6, 11-19, 32, and 33 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the conjugates disclosed in the examples, does not reasonably provide enablement for any conjugates as currently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection was explained in the office action mailed March 7, 2007.

Response to Remarks

6. Applicants' state the specification provides sufficient description in view of the skill in the art, to make and use the claimed invention. Applicants' state the specification describe any number of molecules have been linked to protein transduction domains. Furthermore, a large number of fusogenic domains are known in the art. Methods of conjugating PTDs, fusogenic and heterologous molecules are known in the art. Applicants' cite Michiue et al. to demonstrate that a PTD fused to a p53 protein and a fusogenic domain can be useful to treat cancer. Applicants state the amount of experimentation required to practice the invention is not undue.

Applicant's arguments filed June 11, 2007 have been fully considered but they are not persuasive. The issue in this application is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan, and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F. 2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "... scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skill in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, absent direction/guidance regarding whether the fusion polypeptides identified by functional characteristics can tolerate the covalent conjugation modifications contemplated a non-functional protein polymer may result and one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 31, 34, 35, and 36 are rejected under 35 U.S.C. 102(a) as being anticipated by Navarro-Quiroga et al. (Molecular Brain Research 105: 86-97 (2002)).

The rejection was explained in the office action mailed March 7, 2007 and applies to new claim 36 as well.

Response to Remarks

9. Applicants' state Navarro-Quiroga et al. teach that an HA2-fusogenic peptide linked to an NT-polylysine moiety results in neuronal uptake in "NTRH-bearing neurons" (see abstract). Applicants' state the NT-polylysine is not a protein transduction domain, but rather a targeting domain that binds with an NT receptor bearing cell. Applicants' state the nuclear localization signal as described by Navarro-Quiroga et al. is not a protein transduction domain. Applicants' state that Navrro-Quiroga et al. describes targeting moieties (NT and nuclear localization moiety) linked to a fusogenic domain. Applicants' state Navarro-Quiroga et al. do not teach or suggest a fusogenic domain linked to a protein transduction domain as recited in Applicants' claim 31.

Applicant's arguments filed June 11, 2007 have been fully considered but they are not persuasive. Navarro-Quiroga et al. describe a fusion polypeptide comprising SEQ ID NO: 3 (GLFEAIAEFIEGGWEGLIEG). The peptide is conjugated to Vp1 nuclear localization signal of SV40 and with a neurotensin polypeptide sequence (see page 87, Materials and methods, section 2.1). The peptide sequences assist in the transduction of the fusion molecule and functions as a protein transduction domain, therefore the Vp1 is reasonably interpreted to be a transduction moiety. The fusion construct displayed nuclear localization of the plasmid DNA in neuroblastoma N1E-115 cells (see Abstract).

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

August 30, 2007

AD
/Anand Desai/
Patent Examiner
Art Unit 1656

/Robert B. Mondesi/
Primary Examiner
Art Unit 1652